Set	Items	Description
S1	28898	RESPIRATORY(W)SYNCYTIAL(W)VIRUS
S2	25924	RSV
S3	419	HRSV
S4	2764	SMALL(W)HYDROPHOBIC
S5	132119	SH
S6	44069	S1 OR S2 OR S3
S7	134509	S4 OR S5
S8	449275	VACCINE OR IMMUNOGENIC
S9	1220	S6 AND S7
S10	426	S9 NOT PY>1996
S11	302	RD (unique items)
S12	99	S11 AND S8
S13	18411	S6/TI
S14	314	S13 AND S7
S15	148	S14 NOT PY>1996
S16	40	RD (unique items)
S17	27	S16 NOT S12
S18	1936903	MUTANT? ? OR MUTATION? ? OR MUTATED OR MUTATING
S19	465878	DELETION OR KNOCKOUT
S20	174	S13 AND S18 AND S19
S21	58	S20 NOT PY>1996
S22	28	RD (unique items)
S23	26	S22 NOT (S12 OR S17)
S24	706	AU="MURPHY B"
S25	537	AU="MURPHY B R"
S26	155	AU="MURPHY B."
S27	329	AU="MURPHY B.R."
S28	40	AU="MURPHY BRIAN"
S29	183	AU="MURPHY BRIAN R" OR AU="MURPHY BRIAN ROBERT" OR AU="MURPHY BRIAN ROBERTS"
S30	1945	S24 OR S25 OR S26 OR S27 OR S28 OR S29
S31	320	S6 AND S30
S32	193	S31 NOT PY>1996
S33	99	RD (unique items)
S34	99	S33 NOT (S12 OR S17 OR S23)
S35	1	S34 AND S7
S36	98	S34 NOT S35

?

12/3,AB/4 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00279611
IDENTIFYING NO.: 1Z01BK06003-07 AGENCY CODE: CRISP
VACCINE **EFFICACY: CHARACTERIZATION OF THE PROTECTIVE IMMUNE RESPONSE TO RESPIRAT**
PRINCIPAL INVESTIGATOR: BEELER, JUDY
ADDRESS: , NIH
SPONSORING ORG.: ??
FY : 2000
SUMMARY: **Respiratory syncytial virus** is the most common cause of lower respiratory tract disease in young children worldwide. The F and G glycoproteins of this virus are known to be targets of a protective immune response; however, following natural infection, immunity is incomplete. Repeated infections with viruses of the homologous or heterologous subtypes occur despite high levels of neutralizing antibody. In addition, antibodies that neutralize extracellular virus may not be able to inhibit fusion, allowing cell-to-cell spread of virus. These findings suggest that B cell responses seen following infection may be deficient in antibodies that prevent virus- receptor interactions. In order to better understand the virus-cell interactions required for infection, studies were initiated to more completely define the receptor (s) used by **RSV** . The binding of viral proteins to cell surface glycosaminoclycans was evaluated using heparin agarose affinity chromatography. Studies using whole virions and infected cell lysates showed that both F and G glycoproteins bind to heparin. Vaccinia recombinant viruses expressing individual **RSV** glycoproteins, purified F and G glycoproteins and the strain **RSV** /B cp 52 which expresses F glycoprotein but lacks G and **SH** , showed that F-heparin binding was independent of G. Purified F and G glycoprotein bound to Vero and Hep-2 cells and this interaction was specifically inhibited by heparin, suggesting that these viral glycoproteins bind to cellular homologues of heparin. Likewise, infectivity of subgroup A and B viruses was decreased 60-80% in the presence of heparin, and this inhibition was dose-dependent. In order to identify linear G sequences responsible for heparin binding, overlapping peptides were evaluated for their ability to bind during heparin agarose affinity chromatography. These studies identified a linear sequence on subgroup A G: , and subgroup B G: that bound to heparin. These peptides also bound to Vero and Hep-2 cells and peptide-cell binding was specifically inhibited by heparin in a dose dependent manner suggesting that the interactions occurred between peptides and cell surface glycosaminoglycans. Interestingly, these peptides inhibited homologous and heterologous virus infectivity 60-80% providing evidence that these interactions were biologically important and likely to be involved in the initial steps between virus and cell. Sequence analysis of the **RSV** heparin binding domains showed homology with other mammalian and viral heparin binding domains.

12/3,AB/5 (Item 2 from file: 266)
DIALOG(R)File 266:FEDRIP

00275977
IDENTIFYING NO.: 2R44AI45267-02 AGENCY CODE: CRISP
SELECTION OF RESPRIRATORY SYNCYTIAL VIRUS SUBGROUP A & B VACCINE **CANDIDATES**
PRINCIPAL INVESTIGATOR: JIN, HONG
ADDRESS: AVIRON 297 NORTH BERNARDO AVENUE MOUNTAIN VIEW, CA 94043
PERFORMING ORG.: AVIRON, MOUNTAIN VIEW, CALIFORNIA

SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
FY : 2000
SUMMARY: DESCRIPTION: (Adapted from Applicant's Abstract) **Respiratory Syncytial Virus** (**RSV**), subgroups A and B, are responsible for serious respiratory tract disease in infants, and the elderly and immunocompromised persons. No **vaccine** is currently available and subunit approaches have so far failed. The investigators have utilized recently described "reverse genetic" techniques to construct a unique set of live, recombinant chimeric **RSV vaccine** candidates that express both subgroup A and subgroup B specific surface antigens. Two mutagenesis strategies which they have previously used to attenuate the wild type (WT) **RSV** A2 strain will be used to complete construction of chimeric virus **vaccine** candidates for preclinical testing. Using alanine scanning and cysteine replacement mutagenesis of the **RSV** L gene (RNA-dependent polymerase) the investigators have defined genetic loci that when altered produce a temperature sensitive replication phenotype. Deletion of non-essential genes (**SH** , M2-2, NS1, NS2) will be combined with the L gene ts mutations to produce genetically stable chimeric RS viruses that are non-pathogenic and have unique replication phenotypes. The overall goal of the Phase 1 SBIR grant is to select a chimeric RS virus that is safe, **immunogenic** and protects against WT **RSV** challenge. A Phase 2 SBIR grant will be used to complete preclinical testing in a subhuman primate model and to initiate human clinical trials. PROPOSED COMMERCIAL APPLICATION: The SBIR application should lead to generation of live attenuated **RSV** vaccines. **RSV vaccine** is needed to prevent disease caused by **RSV** infection.

12/3,AB/6 (Item 3 from file: 266)
DIALOG(R)File 266:FEDRIP

00271545
IDENTIFYING NO.: 1Z01AI00372-17 AGENCY CODE: CRISP
REPLICATION,VIRULENCE & IMMUNOGENICITY IN RECOMBINANT RESPIRATORY SYNCYTIAL VIRUS
PRINCIPAL INVESTIGATOR: COLLINS, PETER LEON
ADDRESS: NIAID, NIH
SPONSORING ORG.: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
FY : 2000
SUMMARY: Human **respiratory syncytial virus** (**RSV**) is the most important viral agent of ped iatric respiratory tract disease worldwide and is responsible for a huge burden of morbidity and significant mortality. A licensed **vaccine** remains to be develop ed. Obstacles to **vaccine** development include the poor growth of the virus in cel l culture, the semi-permissive nature of the infection in experimental animals, and the difficulty of achieving an appropriate balance between immunogenicity (w hich depends on reasonable levels of virus replication) and attenuation (which d epends on reduced levels of virus replication). We recently developed a method f or producing infectious recombinant **RSV** by the intracellular coexpression of cDN As encoding a complete **RSV** replicative intermediate RNA (antigenome) and the N, P, L and M2-1 proteins, which together constitute a nucleocapsid that is fully c ompetent for RNA synthesis. This provides an important tool for basic molecular and pathogenesis studies as well as a method for fine- tuning the level of atten uation of candidate **vaccine** viruses. **RSV** encodes ten mRNAs encoding eleven prote ins (the M2 mRNA contains two overlapping ORFs encoding two separate proteins, M 2-1 and M2-2). We investigated whether individual **RSV** genes could be ?knocked ou t? (deleted) without ablating the ability of the virus to grow in cell culture. To date, four **RSV** genes have been individually knocked out without loss of infec tivity, namely NS1, NS2, **SH** , and G. Deletion of the NS2 gene is highly attenuati

ng in vitro and in vivo and represents a very useful mutation for **vaccine** purpos es. The NS1 and **SH** knockout virus are moderately attenuating, and also are candi dates for inclusion in a live-attenuated **vaccine** . The G knockout virus grows wel l in certain cells but not others, implying that it is using an alternative rece ptor whose distribution is cell-specific. The ability to recover a G knockout vi rus shows that G is not essential for the formation or transmission of infectiou s virus, findings which have important implications for virus assembly and recep tor usage. Finally, we previously showed that **RSV** can accept and express an adde d foreign gene. Here, we have expressed certain cytokines in recombinant **RSV** as a possible method to improve the immune response to a live-attenuated **vaccine** . - Virus, **vaccine** , live-attenuated viral **vaccine** , pediatrics, infectious disease, respiratory tract disease, recombinant DNA

12/3,AB/8 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0157084 DBA Accession No.: 93-15136 PATENT
Cold-adapted mutant respiratory- syncytial virus - **attenuation and antigen gene cloning for use as a recombinant** vaccine
PATENT ASSIGNEE: Am.Cyanamid 1993
PATENT NUMBER: EP 567100 PATENT DATE: 931027 WPI ACCESSION NO.: 93-338162 (9343)
PRIORITY APPLIC. NO.: US 871420 APPLIC. DATE: 920421
NATIONAL APPLIC. NO.: EP 93106496 APPLIC. DATE: 930421
LANGUAGE: English
ABSTRACT: A cold-adapted attenuated mutant **respiratory -syncytial virus** (**RSV**) of subgroup A or B is new, e.g. virus 3Ap20E, 3Ap20F, 3Ap28F, 2Bp33F, 2Bp24G, 2Bp20L or 2Bp34L. A purified **immunogenic** polypeptide (e.g. specified polypeptides L, F, G, M, M2(22K), P, **SH** , 1B, 1C or N) is also new, as is nucleic acid encoding the **RSV** polypeptides. The virus, polypeptides and nucleic acids are useful in recombinant vaccines against **RSV** infection. In preferred embodiments, plasmid, vaccinia virus, polio virus, adeno virus and baculo virus vectors for **RSV** protein gene cloning are described. An **RSV** polypeptide gene may be inserted into such a vector with specific initiation signals and transcription-translation control signals and a selectable marker and expressed in e.g. a CHO cell culture, insect cell culture, Escherichia coli, Salmonella sp. or Shigella sp. for recombinant **vaccine** production. The recombinant **RSV** polypeptide may be purified by chromatography, centrifugation, precipitation, etc. (63pp)

12/3,AB/10 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2001 AMERICAN CHEMICAL SOCIETY. All rts. reserv.

120006778 CA: 120(1)6778c PATENT
Mutant respiratory syncytial virus (RSV), vaccines containing it, and methods of vaccination with RSV
INVENTOR(AUTHOR): Randolph, Valerie Bruce; Crowley, Joan Coflan
LOCATION: USA
ASSIGNEE: American Cyanamid Co.
PATENT: European Pat. Appl. ; EP 567100 A1 DATE: 931027
APPLICATION: EP 93106496 (930421) *US 871420 (920421)
PAGES: 63 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C12N-015/45A; C12N-007/08B; C12N-015/87B; A61K-048/00B; C12N-015/86B; A61K-039/155B; C07K-013/00B DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE

12/3,AB/68 (Item 47 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00294413
HRSV VACCINE
VACCIN CONTRE LE VRSH
Patent Applicant/Assignee:
THE UPJOHN COMPANY
NICHOLAS Judith A
Inventor(s):
NICHOLAS Judith A
Patent and Priority Information (Country, Number, Date):
Patent: WO 9204375 A1 19920319
Application: WO 91US5255 19910730 (PCT/WO US9105255)
Priority Application: US 90575892 19900831
Designated States: AT AU BB BE BF BG BJ BR CA CF CG CH CI CM CS DE DK ES FI FR GA GB GN GR JP KP KR LK LU MC MG ML MN MR MW NL NO PL RO SD SE SN SU TD TG US
Publication Language: English
Fulltext Word Count: 7154

English Abstract
Peptides useful for protecting humans from Human **Respiratory Syncytial Virus** infection is disclosed. Vaccines comprising the peptides and a method of protecting humans from **HRSV** infection are disclosed.

Japanese Abstract
On decrit des peptides utiles a la protection des humains contre l'infection par le Virus Respiratoire Syncytial Humain. On decrit aussi des vaccins comprenant ces peptides et un procede destine a proteger les humains contre l'infection par le VRSH.
?

17/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07916042 94233745
Analysis of respiratory syncytial virus **F, G, and** SH **proteins in cell fusion.**
Heminway BR; Yu Y; Tanaka Y; Perrine KG; Gustafson E; Bernstein JM; Galinski MS
Department of Molecular Biology, Cleveland Clinic Foundation, Ohio 44195.
Virology (UNITED STATES) May 1 1994, 200 (2) p801-5, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Recombinant expression of the human respiratory syncytial virus (RSV) fusion (F) glycoprotein, receptor-binding glycoprotein (G), and **small hydrophobic** (**SH**) protein was performed to determine the role(s) of these proteins in syncytia formation. These studies used a vaccinia virus expressing the bacteriophage (T7) RNA polymerase gene and plasmid vectors containing the RSV genes under the control of a T7 promoter. Within the context of this expression system, expression of any individual RSV gene, or coexpression of F+G genes, did not elicit the formation of syncytia. However, at plasmid input levels which were 10-fold higher than those normally used, coexpression of F+G induced low but detectable levels of cell fusion. In contrast, coexpression of F, G, and **SH** together elicited extensive cell fusion resembling that of an authentically infected cell monolayer. In addition, coexpression of F and **SH** elicited significant cell fusion, although to a lesser extent than was observed when G was included. Cell fusion induced by coexpression of F+**SH** was found to be specific to the RSV proteins, since coexpression of **SH** with the analogous F proteins from human parainfluenza virus type 3, human parainfluenza virus type 2, Sendai virus, or simian virus type 5 (SV5) did not elicit cell fusion. Finally, coexpression of the SV5 **SH** protein with the RSV or SV5 glycoproteins also failed to induce syncytia, suggesting type-specific restrictions between the two sets of viral proteins.

17/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07607901 93367411
Antibody responses of children to the C-terminal peptide of the SH **protein of** respiratory syncytial virus **and the immunological characterization of this protein.**
Akerlind-Stopner B; Hu A; Mufson MA; Utter G; Norrby E
Department of Virology, Karolinska Institute, School of Medicine, Stockholm, Sweden.
Journal of medical virology (UNITED STATES) Jun 1993, 40 (2) p112-20, ISSN 0146-6615 Journal Code: I9N
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The **SH** protein of RSV, a small integrated hydrophobic membrane protein, consists of 64 amino acid residues in the polypeptide of subgroup A and 65 amino acid residues in the polypeptide of subgroup B. We synthesized five peptides, representing the **SH** protein of each RSV subgroup comprised of the following amino acid residues: 2-16, 12-26, 35-49, 45-60, and for subgroup A, 51-64 and for subgroup B, 51-65. Peptides 2-16 and 51-64/65 represented the N-terminal and C-terminal ends of the protein, respectively. In RIPA, under reducing conditions with mercaptoethanol, hyperimmune guinea pig (GP) serum against C-terminal peptide of the two

subgroups precipitated the homologous 7.5 kDa and 21-30 kDa **SH** proteins. Under nonreducing conditions, the GP antipeptide sera precipitated all three **SH** proteins, suggesting that the 13-15 kDa protein exists as a dimer. The subgroup A 7.5 and 13-15 kDa proteins had apparent molecular weights about 1-2 kDa higher than the corresponding subgroup B proteins. The C-terminal peptides of subgroups A and B were used to characterize the immune response of 11 children, age 1 month to 1 year, with presumed primary RSV infection. Three of 4 children with subgroup A infection and 4 of 7 children with subgroup B infection developed homologous 4-fold rises in antibody to C-terminal peptide (aa 51-64/65) during convalescence. Except for one child with subgroup A and one child with subgroup B infection, the other 5 children developed heterologous rises also. (ABSTRACT TRUNCATED AT 250 WORDS)

17/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07587496 93329397
Membrane orientation and oligomerization of the small hydrophobic **protein of human** respiratory syncytial virus.
Collins PL; Mottet G
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
Journal of general virology (ENGLAND) Jul 1993, 74 (Pt 7) p1445-50, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Previous work has demonstrated that the **small hydrophobic** (**SH**) protein of human respiratory syncytial virus (RSV) A2 strain is a 64 amino acid integral membrane protein that accumulates intracellularly as an unglycosylated major species (SH0), a minor species truncated at the amino terminus and two N-glycosylated species one of which contains a further addition of polylactosamine. In this study, the membrane orientation of SH0 was mapped by trypsinization of intact RSV-infected cells followed by washout, lysis and immunoprecipitation of protected fragments with antisera specific for the protein termini. This showed that the C terminus is extracellular and the **SH** protein was not detectably palmitylated. Analysis of the **SH** protein by sedimentation on sucrose gradients showed that it rapidly assembles into a homo-oligomer that co-sediments with the F protein tetramer. Interestingly, all forms of the **SH** protein were found in the oligomeric fraction. Chemical cross-linking generated species which appeared to represent dimers, trimers, tetramers and pentamers as well as a minor species of 180K which might correspond to the oligomeric form detected by sucrose gradient sedimentation.

17/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07354711 91132131
Respiratory syncytial virus **heterogeneity during an epidemic: analysis by limited nucleotide sequencing (SH gene) and restriction mapping (N gene).**
Cane PA; Pringle CR
Department of Biological Sciences, University of Warwick, Coventry, U.K.
Journal of general virology (ENGLAND) Feb 1991, 72 (Pt 2) p349-57, ISSN 0022-1317 Journal Code: I9B

Languages: ENGLISH
Document type: JOURNAL ARTICLE
The genes encoding the **small hydrophobic** (**SH**) proteins of a series of respiratory syncytial (RS) virus strains were amplified using the polymerase chain reaction, cloned and sequenced. Analysis of the **SH** gene sequences from 12 RS virus strains isolated between 1956 and 1989 confirmed the homogeneity of the two subgroups. A and B, previously defined serologically. Although there is only 76% deduced amino acid sequence identity of **SH** proteins between subgroups, there was little variation in deduced amino acid sequences within the subgroups; nucleotide homologies within the subgroups ranged between 93% and 99%. Forty-two isolates of RS virus from a single epidemic season (autumn/winter 1989) were also examined to determine their relatedness. For these isolates regions of both the **SH** and nucleocapsid protein genes of each isolate were amplified and these regions were further analysed by direct nucleotide sequencing or restriction mapping. It was possible to discriminate at least six different lineages (or substrains) of RS virus circulating at the same time and in the same locality.

17/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07145241 93033134
Polylactosaminoglycan modification of the respiratory syncytial virus small hydrophobic **(SH) protein: a conserved feature among human and bovine respiratory syncytial viruses.**
Anderson K; King AM; Lerch RA; Wertz GW
Department of Microbiology, University of Alabama, Birmingham 35294.
Virology (UNITED STATES) Nov 1992, 191 (1) p417-30, ISSN 0042-6822 Journal Code: XEA
Contract/Grant No.: R37 AI12464, AI, NIAID; AI20181, AI, NIAID; T32-HL07553, HL, NHLBI; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We investigated the nature of the oligosaccharide modification of the glycosylated forms of the **small hydrophobic** integral membrane protein, **SH** (previously designated 1A), of respiratory syncytial (RS) virus. Analysis of **SH** protein expressed in cells infected with RS virus or with a recombinant vaccinia virus revealed two glycosylated **SH** protein species, SHg and SHp, which contained N-linked carbohydrate residues. SHp migrated diffusely on polyacrylamide gels, which suggested modification by polylactosaminoglycan oligosaccharides. Polylactosaminoglycan modification of SHp was established from three lines of investigation: (1) the synthesis of SHp in a cell line (IdID) conditionally defective in the ability to add specific carbohydrate residues to N- or O-linked oligosaccharide chains required the addition of galactose, which is a component of the N-acetyllactosamine repeating unit; (2) SHp was sensitive to digestion with endo-beta-galactosidase, which cleaves the beta 1-4 linkage between galactose and N-acetylglucosamine of the repeated N-acetyllactosamine subunit; and (3) SHp was selected by Datura stramonium lectin (Dsl), which has specificity for polylactosaminoglycans. The presence of SHp as a component of purified human subgroups A and B and bovine RS virus particles was demonstrated by Dsl affinity selection. In addition to SHp, nonglycosylated SHo was selected by Dsl affinity, indicating that SHp and SHo may associate to form complexes within infected cells and virus particles. To identify conserved amino acid residues among the human and bovine **SH** glycoproteins that may function as signals for polylactosaminoglycan modification, the nucleotide sequences of the **SH** protein genes of a human subgroup B virus (8/60) and a bovine virus (391-2)

were determined and compared to those of a human subgroup A virus (A2), a subgroup B virus (18537), and a bovine virus (A51908). A comparison of the deduced amino acid sequences of the human and bovine RS virus **SH** proteins indicated that a central hydrophobic region and the presence of potential N-linked glycosylation sites on either side of the central hydrophobic region were conserved features that may be required for the polylactosaminoglycan modification of **SH** .

17/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06424308 90324943
The small hydrophobic **protein of human** respiratory syncytial virus: **comparison between antigenic subgroups A and B.**
Collins PL; Olmsted RA; Johnson PR
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
Journal of general virology (ENGLAND) Jul 1990, 71 (Pt 7) p1571-6, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The nucleotide and amino acid sequences of the mRNA and predicted polypeptide of the integral membrane **small hydrophobic** (**SH**) protein of human respiratory syncytial virus strain 18537 (a prototype strain of antigenic subgroup B) were determined from cloned cDNA. At the nucleotide and amino acid levels there was 78% and 76% identity, respectively, with the previously described **SH** mRNA and protein of strain A2 (a prototype strain of subgroup A). Most of the amino acid substitutions occurred in the predicted ectodomain (50% identity). The pattern of posttranslational processing of the strain 18537 **SH** protein was very similar to that of strain A2, yielding a nonglycosylated form and two glycosylated forms. Analysis of released virions of strain A2 by immunoprecipitation with **SH** -specific antibodies suggested that the major non-glycosylated species and one of the glycosylated species are virion structural components.

17/3,AB/21 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03125922 Genuine Article#: NG523 Number of References: 40
Title: ANALYSIS OF RESPIRATORY SYNCYTIAL VIRUS **F-PROTEIN, G-PROTEIN, AND** SH-**PROTEIN IN CELL-FUSION** (Abstract Available)
Author(s): HEMINWAY BR; YU Y; TANAKA Y; PERRINE KG; GUSTAFSON E; BERNSTEIN JM; GALINSKI MS
Corporate Source: CLEVELAND CLIN FDN,RES INST,DEPT MOLEC BIOL/CLEVELAND//OH/44195; CLEVELAND CLIN FDN,RES INST,DEPT MOLEC BIOL/CLEVELAND//OH/44195; WRIGHT STATE UNIV,VET ADM MED CTR/DAYTON//OH/45428
Journal: VIROLOGY, 1994, V200, N2 (MAY 1), P801-805
ISSN: 0042-6822
Language: ENGLISH Document Type: NOTE
Abstract: Recombinant expression of the human respiratory syncytial virus (RSV) fusion (F) glycoprotein, receptor-binding glycoprotein (G), and **small hydrophobic** (**SH**) protein was performed to determine the role(s) of these proteins in syncytia formation. These studies used a vaccinia virus expressing the bacteriophage (T7) RNA polymerase gene and plasmid vectors containing the RSV genes under the control of a T7

promoter. Within the context of this expression system, expression of any individual RSV gene, or coexpression of F + G genes, did not elicit the formation of syncytia. However, at plasmid input levels which were 10-fold higher than those normally used, coexpression of F + G induced low but detectable levels of cell fusion. In contrast, coexpression of F, G, and **SH** together elicited extensive cell fusion resembling that of an authentically infected cell monolayer. In addition, coexpression of F and **SH** elicited significant cell fusion, although to a lesser extent than was observed when G was included. Cell fusion induced by coexpression of F + **SH** was found to be specific to the RSV proteins, since coexpression of **SH** with the analogous F proteins from human parainfluenza virus type 3, human parainfluenza virus type 2, Sendai virus, or simian Virus type 5 (SV5) did not elicit cell fusion. Finally, coexpression of the SV5 **SH** protein with the RSV or SV5 glycoproteins also failed to induce syncytia, suggesting type-specific restrictions between the two sets of viral proteins.

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23/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08706026 96145140
Definition and functional analysis of the signal/anchor domain of the human respiratory syncytial virus **glycoprotein G.**
Lichtenstein DL; Roberts SR; Wertz GW; Ball LA
Department of Biochemistry, University of Wisconsin-Madison 53706, USA.
Journal of general virology (ENGLAND) Jan 1996, 77 (Pt 1) p109-18, ISSN 0022-1317 Journal Code: I9B
Contract/Grant No.: R37 AI 18270, AI, NIAID; R37 AI 12464, AI, NIAID; AI 20181, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The attachment protein G of human respiratory syncytial (RS) virus is a type II transmembrane glycoprotein. A secreted from of the G protein is also produced. To examine the two distinct hydrophobic regions in the N-terminal 63 amino acids of G protein for their role(s) in membrane insertion and anchoring, transport to the cell surface, and secretion, G proteins that contained point **mutations** or deletions were synthesized by cell-free transcription-translation and in cells by expression from recombinant vaccinia virus vectors. A **mutant** protein lacking the entire major hydrophobic region (amino acids 38-63) was not glycosylated, not expressed on the cell surface, and not secreted, because it was not inserted into membranes. In contrast, **deletion** of the minor hydrophobic region (amino acids 23-31) had no detectable effect on membrane insertion or anchoring. These data provided direct evidence that amino acids 38-63 were necessary for membrane insertion and contained the signal/anchor domain of RS virus G protein. **Mutant** proteins that lacked either the N-terminal or the C-terminal half of this 26 residue hydrophobic region were inserted into membranes and processed to maturity, showing that either half of this region was sufficient for membrane insertion. However, these two **mutant** proteins were secreted more abundantly than wild-type G protein. We propose that their truncated hydrophobic domains interacted with membranes in a way that mimicked the N-terminal signal sequence of naturally secreted proteins, allowing proteolytic cleavage of the **mutant** proteins.

23/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08660728 96135189
Identification of protein regions involved in the interaction of human respiratory syncytial virus **phosphoprotein and nucleoprotein: significance for nucleocapsid assembly and formation of cytoplasmic inclusions.**
Garcia-Barreno B; Delgado T; Melero JA
Instituto de Salud Carlos III, Centro Nacional de Biologia Celular y Retrovirus, Madrid, Spain.
Journal of virology (UNITED STATES) Feb 1996, 70 (2) p801-8, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have reported previously that the nucleoprotein (N), the phosphoprotein (P), and the 22-kDa protein of human respiratory syncytial virus (HRSV) are components of the cytoplasmic inclusion bodies observed in HEp-2-infected cells. In addition, coexpression of N and P was sufficient

to induce the formation of N-P complexes detectable by either coimmunoprecipitation with anti-P antibodies or generation of cytoplasmic inclusions. We now report the identification of protein regions required for these interactions. **Deletion mutant** analysis of the P protein gene indicated that its C-terminal end was essential for interacting with N. This conclusion was strengthened by the finding that an anti-P monoclonal antibody (021/12P), reacting with a 21-residue P protein C-terminal peptide, apparently displaced N from N-P complexes. The same effect was observed with high concentrations of the C-terminal peptide. However, sequence requirements for the P protein C-terminal end were not absolute, and **mutants** with the substitution Ser-237-->Ala or Ser-237-->Thr were as efficient as the wild type in interacting with N. In addition, P and N proteins from strains of different HRSV antigenic groups, with sequence differences in the P protein C-terminal end, were able to coimmunoprecipitate and formed cytoplasmic inclusions. **Deletion mutant** analysis of the N gene indicated that large segments of this polypeptide were required for interacting with P. The relevance of these interactions for HRSV is discussed in comparison with those of analogous proteins from related viruses.

23/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07979601 94335058
Oligo(A) sequences of human respiratory syncytial virus **G protein gene: assessment of their genetic stability in frameshift** mutants.
Garcia-Barreno B; Delgado T; Melero JA
Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Madrid, Spain.
Journal of virology (UNITED STATES) Sep 1994, 68 (9) p5460-8, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have described previously antibody-resistant **mutants** of the human respiratory syncytial virus Long strain that contained frameshift changes generated by deletions or insertions of a single adenosine in oligo(A) tracts (mRNA sense) of the G protein gene. Since these **mutations** introduced drastic structural and antigenic changes in the G protein C-terminal third, we decided to test the **mutant** stability by passaging the viruses in either the presence or the absence of selective antibody. Two such **mutants** (R63/1/2/3 and R63/2/4/8), with a single reading frame shift, reverted after a few passages in the absence of antibody to the wild-type genotype, by insertion of an A at the same homopolymeric tract as in the original **deletion** . In contrast, a double frameshift **mutant** (R63/2/4/1), generated by **deletion** of an A after nucleotide 623 and insertion of another A seven triplets later, was stably maintained after passage in either the absence or the presence of antibody. The stability of this **mutant** was manifested in its capacity to gradually displace the Long strain from mixed infections and by the fact that **mutant** R63/2/4/8 acquired the genotype of R63/2/4/1 after several passages in the presence of antibody. These results were indicative of genetic instability in the oligo(A) tract length of certain G protein **mutants** , which resulted in frameshift changes. The frequency of such errors among the viral RNA population obtained from a single infectious cycle was estimated to be lower than 1%. The relevance of these results for respiratory syncytial virus evolution is discussed.

23/3,AB/8 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05391162 Genuine Article#: VV421 Number of References: 25
Title: NUCLEOTIDE-SEQUENCE ANALYSIS OF THE RESPIRATORY SYNCYTIAL VIRUS **SUBGROUP A COLD-PASSAGED (CP) TEMPERATURE-SENSITIVE (TS) CPTS-248/404 LIVE ATTENUATED VIRUS-VACCINE CANDIDATE** (Abstract Available)
Author(s): FIRESTONE CY; WHITEHEAD SS; COLLINS PL; MURPHY BR; CROWE JE
Corporate Source: NIAID,RESP VIRUSES SECT,INFECT DIS LAB,NIH,7 CTR DR,MSC-9720/BETHESDA//MD/20892; NIAID,RESP VIRUSES SECT,INFECT DIS LAB,NIH/BETHESDA//MD/20892
Journal: VIROLOGY, 1996, V225, N2 (NOV 15), P419-422
ISSN: 0042-6822
Language: ENGLISH Document Type: ARTICLE
Abstract: The complete nucleotide sequence of the RSV cpts-248/404 live attenuated vaccine candidate was determined from cloned cDNA and was compared to that of the RSV A2/HEK7 wild-type, cold-passaged cp-RSV, and cpts-248 virus, which constitute the series of progenitor viruses. RSV cpts-248/404 is more attenuated and more temperature sensitive (ts) (shut-off temperature 36 degrees) than its cpts-248 parent virus (shut-off temperature 38 degrees) and is currently being evaluated in phase I clinical trials in humans. Our ultimate goal is to identify the genetic basis for the host range attenuation phenotype exhibited by cp-RSV (i.e., efficient replication in tissue culture but decreased replication in chimpanzees and humans) and for the ts and attenuation phenotypes of its chemically mutagenized derivatives, cpts-248 and cpts-248/404. Compared with its cpts-248 parent, the cpts-248/404 virus possesses an amino acid change in the polymerase (L) protein and a single nucleotide substitution in the M2 gene start sequence. In total, the cpts-248/404 **mutant** differs from its wild-type RSV A2/HEK7 progenitor in seven amino acids [four in the polymerase (L) protein, two in the fusion (F) glycoprotein, and one in the (N) nucleoprotein] and one nucleotide difference in the M2 gene start sequence. Heterogeneity at nucleotide position 4 (G or C, negative sense, compared to G in the RSV A2/HEK7 progenitor) in the leader region of vRNA developed during passage of the cpts-248/404 in tissue culture. Biologically cloned derivatives of RSV cpts-248/404 virus that differed at position 4 possessed the same level of temperature sensitivity and exhibited the same level of replication in the upper and lower respiratory tract of mice, suggesting that heterogeneity at this position is not clinically relevant. The determination of the nucleotide sequence of the cpts-248/404 virus will allow evaluation of the stability of the eight **mutations** that are associated with the attenuation phenotype during vaccine production and following replication in humans. (C) 1996 Academic Press, Inc.

23/3,AB/9 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05084164 Genuine Article#: TP526 Number of References: 45
Title: IDENTIFICATION OF PROTEIN REGIONS INVOLVED IN THE INTERACTION OF HUMAN RESPIRATORY SYNCYTIAL VIRUS **PHOSPHOPROTEIN AND NUCLEOPROTEIN - SIGNIFICANCE FOR NUCLEOCAPSID ASSEMBLY AND FORMATION OF CYTOPLASMIC INCLUSIONS** (Abstract Available)
Author(s): GARCIABARRENO B; DELGADO T; MELERO JA
Corporate Source: CTR NACL BIOL CELULAR & RETROVIRUS,INST SALUD CARLOS 3/E-28220 MADRID//SPAIN/; CTR NACL BIOL CELULAR & RETROVIRUS,INST SALUD CARLOS 3/E-28220 MADRID//SPAIN/
Journal: JOURNAL OF VIROLOGY, 1996, V70, N2 (FEB), P801-808

ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: We have reported previously that the nucleoprotein (N), the phosphoprotein (P), and the 22-kDa protein of human respiratory syncytial virus (HRSV) are components of the cytoplasmic inclusion bodies observed in HEp-2-infected cells, In addition, coexpression of N and P was sufficient to induce the formation of N-P complexes detectable by either coimmunoprecipitation with anti-P antibodies or,generation of cytoplasmic inclusions, We now report the identification of protein regions required for these interactions, **Deletion mutant** analysis of the P protein gene indicated that its C-terminal end was essential for interacting with N. This conclusion was strengthened by the finding that an anti-P monoclonal antibody (021/12P), reacting with a 21-residue P protein C-terminal peptide, apparently displaced N from N-P complexes, The same effect was observed with high concentrations of the C-terminal peptide, However, sequence requirements for the P protein C-terminal end were not absolute, and **mutants** with the substitution Ser-237-->Ala or Ser-237-->Thr were as efficient as the wild type in interacting with N, In addition, P and N proteins from strains of different HRSV antigenic groups, with sequence differences in the P protein C-terminal end, were able to coimmunoprecipitate and formed cytoplasmic inclusions, **Deletion mutant** analysis of the N gene indicated that large segments of this polypeptide were required for interacting with P, The relevance of these interactions for HRSV is discussed in comparison with those of analogous proteins from related viruses.

23/3,AB/11 (Item 1 from file: 65)

01511696 INSIDE CONFERENCE ITEM ID: CN015007038
In vitro assembly of virus-like particles with RSV **Gag** deletion mutants
Campbell, S.; Vogt, V. M.
CONFERENCE: Retroviruses-Meeting
ABSTRACTS OF PAPERS PRESENTED AT THE MEETING ON RETROVIRUSES, 1996 P: 361
Cold Spring Harbor Laboratory, 1996
LANGUAGE: English DOCUMENT TYPE: Conference Abstracts and programme
CONFERENCE SPONSOR: Cold Spring Harbor Laboratory (CSH)
CONFERENCE LOCATION: Cold Spring Harbor, NY
CONFERENCE DATE: May 1996 (19960) (19960)

23/3,AB/18 (Item 1 from file: 357)

0181500 DBA Accession No.: 95-05717
Current approaches to the development of vaccines against disease caused by respiratory- syncytial virus **(RSV) and parainfluenza virus (PIV) - a meeting report of the WHO program for vaccine development; attenuation, recombinant vaccine construction and genetic immunization (conference report)**
AUTHOR: Crowe Jr J E
CORPORATE AFFILIATE: Nat.Inst.Allergy+Infec.Dis.Bethesda Nat.Inst.Health-Bethesda
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892, USA.

JOURNAL: Vaccine (13, 4, 415-21) 1995
ISSN: 0264-410X CODEN: VACCDE
CONFERENCE PROCEEDINGS: WHO Programme for Vaccine Development, Workshop, Nyon, Switzerland, 27 March, 1994.
LANGUAGE: English
ABSTRACT: Vaccine production against respiratory-syncytial (RSV) and parainfluenza virus-3 (PIV3) was discussed, with respect to: vaccine candidates; live attenuated strains (Jennerian approach, cold-adapted **mutants** of PIV3 and cold-passaged ts **mutants** of RSV); subunit vaccine candidates (purified virus protein and bacterial expression of virus protein); recombinant vaccine candidates; genetic immunization; reverse genetics (Sendai virus, measles virus and RSV, and PIV3; and an update on the WHO reagent bank. Vaccinia virus recombinants expressing RSV surface glycoproteins have been successfully used as immunogens in chimpanzees. Studies on genetic immunization with influenza virus hemagglutinin or nucleoprotein genes may be extended to immunization strategies with RSV or PIV3. Engineering of the viral genome should allow generation of new types of attenuating **mutations** (e.g. **deletion** , insertion or substitution), or introduction of heterologous genes for generation of multivalent recombinant vaccines. (21 ref)

23/3,AB/19 (Item 2 from file: 357)

0074673 DBA Accession No.: 88-05522
Live viral vaccines for respiratory and enteric tract diseases- caused by rota virus, bovine parainfluenza virus type 3, human influenza-A virus, avian influenza virus and respiratory- syncytial virus
AUTHOR: Chanock R M; Murphy B R; Collins P L; Coelingh K V W; Olmsted R A; Snyder M H
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institute of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Vaccine (6, 2, 129-33) 1988
CODEN: VACCDE
LANGUAGE: English
ABSTRACT: Current attempts to develop satisfactorily attenuated viruses for use as vaccines against enteric tract and respiratory diseases caused by rota virus, bovine parainfluenza type 3 (PIV3) virus, avian X human influenza-A virus, respiratory-syncytial virus are described. The classical approach of Jenner has been updated to incorporate the techniques of contemporary viral genetics, molecular biology and immunology and these modified methods are described for rota viruses, bovine PIV3 and avian X human influenza A virus reassortants. The use of naturally attenuated human viruses, rota viruses, spontaneous or experimentally produced **deletion mutants** , experimentally produced or selected point **mutations** , cold adapted influenza-A virus **mutant** , attenuated viral vectors expressing genes coding for protective antigens or other viruses and respiratory-syncytial viruses are discussed. (20 ref)

23/3,AB/22 (Item 1 from file: 349)

00445016
NUCLEIC ACID RESPIRATORY SYNCYTIAL VIRUS **VACCINES**
VACCINS A ACIDES NUCLEIQUES DU VIRUS RESPIRATOIRE SYNCYTIAL

Patent Applicant/Assignee:
CONNAUGHT LABORATORIES LIMITED
LI Xiaomao
EWASYSHYN Mary E
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Inventor(s):
LI Xiaomao
EWASYSHYN Mary E
SAMBHARA Suryaprakash
KLEIN Michel H
Patent and Priority Information (Country, Number, Date):
Patent: WO 9640945 A2-A3 19961219
Application: WO 96CA398 19960607 (PCT/WO CA9600398)
Priority Application: US 95476397 19950607
Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR TD TG
Publication Language: English
Fulltext Word Count: 12090

English Abstract
Vectors containing a nucleotide sequence coding for an F protein of respiratory syncytial virus (RSV) and a promoter for such sequence, preferably a cytomegalovirus promoter, are described. Such vectors also may contain a further nucleotide sequence located adjacent to the RSV F protein encoding sequence to enhance the immunoprotective ability of the RSV F protein when expressed in vivo. Such vectors may be used to immunize a host, including a human host, by administration thereto. Such vectors also may be used to produce antibodies for detection of RSV infection in a sample.

Japanese Abstract
L'invention concerne des vecteurs qui contiennent une sequence de nucleotides codant une proteine F du virus respiratoire syncytial et un promoteur de cette sequence, de preference un promoteur de cytomegalovirus. Ces vecteurs peuvent egalement contenir une sequence supplementaire de nucleotides adjacente a la sequence codant la proteine F du virus respiratoire syncytial afin d'ameliorer la capacite immunoprotectrice de la proteine F du virus respiratoire syncytial exprimee in vivo. On peut administrer ces vecteurs a un hote, y compris a un hote humain, pour l'immuniser. On peut egalement utiliser ces vecteurs pour produire des anticorps pour detecter l'infection par le virus respiratoire syncytial dans un echantillon.
?

35/3,AB,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07566964 BIOSIS NO.: 000091107518
RESPIRATORY SYNCYTIAL VIRUS RSV **F G M2 22K AND N PROTEINS EACH INDUCE RESISTANCE TO** RSV **CHALLENGE BUT RESISTANCE INDUCED BY M2 AND N PROTEINS IS RELATIVELY SHORT-LIVED**
AUTHOR: CONNORS M; COLLINS P L; FIRESTONE C-Y; **MURPHY B R**
AUTHOR ADDRESS: LABORATORY INFECTIOUS DISEASES, NATIONAL INSTITUTE ALLERGY INFECTIOUS DISEASES, BUILDING 7, ROOM 100, BETHESDA, MD. 20892.
JOURNAL: J VIROL 65 (3). 1991. 1634-1637. 1991
FULL JOURNAL NAME: Journal of Virology
CODEN: JOVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The ability of recombinant vaccinia viruses that separately encoded 9 of the 10 known **respiratory syncytial virus** (**RSV**) proteins to induce resistance to **RSV** challenge was studied in BALB/c mice. Resistance was examined at two intervals following vaccination to examine early (day 9) as well as late (day 28) immunity. BALB/c mice were inoculated simultaneously by the intranasal and intraperitoneal routes with a recombinant vaccinia virus encoding one of the following **RSV** proteins: F, G, N, P, **SH** , M, 1B, 1c, or M2 (22K). A parainfluenza virus type 3 HN protein recombinant (Vac-HN) served as a negative control. One half of the mice were challenged with **RSV** intranasally on day 9, and the remaining animals were challenged on day 28 postvaccination. Mice previously immunized by infection with **RSV** , Vac-F, or Vac-G were completely or almost completely resistant to **RSV** challenge on both days. In contrast, immunization with Vac-HN, -P, -**SH** , -M, -1B, or -1C did not induce detectable resistant to **RSV** challenge. Mice previously infected with Vac-M2 or Vac-N exhibited significant but not complete resistance on day 9. However, in both cases resistance had largely waned by day 28 and was detectable only in mice immunized with Vac-M2. These results demonstrate that F and G proteins expressed by recombinant vaccinia viruses are the most effective **RSV** protective antigens. This study also suggests that **RSV** vaccines need only contain the F and G glycoproteins, because the immunity conferred by the other proteins is less effective and appears to wane rapidly with time.

1991

RESPIRATORY SYNCYTIAL VIRUS RSV **F G M2 22K AND N PROTEINS EACH INDUCE RESISTANCE TO** RSV **CHALLENGE BUT RESISTANCE INDUCED BY M2 AND N PROTEINS IS RELATIVELY SHORT-LIVED**
AUTHOR: CONNORS M; COLLINS P L; FIRESTONE C-Y; **MURPHY B R**

ABSTRACT: The ability of recombinant vaccinia viruses that separately encoded 9 of the 10 known **respiratory syncytial virus** (**RSV**) proteins to induce resistance to **RSV** challenge was studied in BALB/c mice. Resistance was examined at two intervals following vaccination...

...the intranasal and intraperitoneal routes with a recombinant vaccinia virus encoding one of the following **RSV** proteins: F, G, N, P, **SH** , M, 1B, 1c, or M2 (22K). A parainfluenza virus type 3 HN protein recombinant (Vac-HN) served as a negative control. One half of the mice were challenged with **RSV** intranasally on day 9, and the remaining animals were challenged on day 28 postvaccination. Mice previously immunized by infection with **RSV** , Vac-F, or Vac-G were completely or almost completely resistant to **RSV** challenge on both days. In contrast,

immunization with Vac-HN, -P, -**SH** , -M, -1B, or -1C did not induce detectable resistant to **RSV** challenge. Mice previously infected with Vac-M2 or Vac-N exhibited significant but not complete...

...demonstrate that F and G proteins expressed by recombinant vaccinia viruses are the most effective **RSV** protective antigens. This study also suggests that **RSV** vaccines need only contain the F and G glycoproteins, because the immunity conferred by the...

?

36/3,AB/9 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09796821 BIOSIS NO.: 199598251739
Live attenuated mutants of respiratory syncytial virus **(RSV): In vitro markers and replication in mice or chimpanzees correlate with level of attenuation for seronegative human infants.**
AUTHOR: Crowe James E Jr(a); Bui Phuong T(a); Karron Ruth A; Clements Mary Lou; Wright Peter F; Chanock Robert M(a); **Murphy Brian R** (a
AUTHOR ADDRESS: (a)Lab. Infect. Dis., NIH, Bethesda, MD**USA
JOURNAL: Pediatric Research 37 (4 PART 2):p172A 1994
CONFERENCE/MEETING: 105th Annual Meeting of the American Pediatric Society and the 64th Annual Meeting of the Society for Pediatric Research San Diego, California, USA May 7-11, 1995
ISSN: 0031-3998
RECORD TYPE: Citation
LANGUAGE: English
1994

36/3,AB/10 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09749651 BIOSIS NO.: 199598204569
Progress toward the development of a live attenuated respiratory syncytial virus **(RSV) vaccine.**
AUTHOR: **Murphy Brian R** (a); Crowe James E Jr(a); Bui Phuong T(a); Elkins William R(a); Firestone Cai-Yen(a); Chanock Robert M(a); Lubeck Michael D ; Karron Ruth; Clements Mary Lou; Wright Peter F; Siber George R
AUTHOR ADDRESS: (a)Natl. Inst. Health, NIAID, Bethesda, MD 20892-0702**USA
JOURNAL: Journal of Cellular Biochemistry Supplement 0 (19A):p274 1995
CONFERENCE/MEETING: Keystone Symposium on Molecular Aspects of Viral Immunity Keystone, Colorado, USA January 16-23, 1995
ISSN: 0733-1959
RECORD TYPE: Citation
LANGUAGE: English
1995

36/3,AB/11 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09696672 BIOSIS NO.: 199598151590
Live attenuated vaccines for respiratory syncytial virus **and parainfluenza virus type 3.**
BOOK TITLE: Strategies for pediatric vaccines: Conventional and molecular approaches
AUTHOR: **Murphy Brian R** (a); Crowe James E Jr; Lubeck Michael D; Hsu Kuo-Hom Lee; Hall Susan L; Karron Ruth A; Clements Mary Lou; Wright Peter F; Belshe Robert B; Chanock Robert M
BOOK AUTHOR/EDITOR: Redfern D E: Ed
AUTHOR ADDRESS: (a)Respir. Viruses Sect., Lab. Infectious Diseases, National Inst. Allergy Infectious Diseases, Nat**USA
p173-178 1994
BOOK PUBLISHER: Ross Products Division, Abbott Laboratories, 625 Cleveland Avenue, Columbus, Ohio 43216, USA
CONFERENCE/MEETING: 104th Ross Conference on Pediatric Research San Diego, California, USA September 18-21, 1993

RECORD TYPE: Citation
LANGUAGE: English
1994

36/3,AB/17 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09355091 BIOSIS NO.: 199497363461
Satisfactorily attenuated and protective mutants derived from a partially attenuated cold-passaged respiratory syncytial virus **mutant by introduction of additional attenuating mutations during chemical mutagenesis.**
AUTHOR: Crowe James E Jr(a); Bui Phuong T; London William T; Davis Alan R; Hung Paul P; Chanock Robert M; **Murphy Brian R**
AUTHOR ADDRESS: (a)Repiratory Virsues Section, Lab. Infectious Diseases, Natl. Inst. Allergy Infectious Diseases, N**USA
JOURNAL: Vaccine 12 (8):p691-699 1994
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A cold-passaged **RSV** mutant, designated cp-**RSV** , while acquired host range mutations during 52 passages at low temperature in bovine tissue culture, was completely attenuated for seropositive adults and children but retained the capacity to cause upper respiratory disease in seronegative infants. We sought to introduce additional attenuating mutations, such as temperature-sensitive (t) and small-plaque (sp) mutations, into the cp-**RSV** mutant, which is a ts + virus, in order to generate a mutant which would be satisfactorily attenuated in seronegative infants and young children. Nine mutants of cp-**RSV** , which had acquired either the ts or small-plaque sp phenotype, were generated by chemical mutagenesis with 5-fluorouracil. The two ts mutants with the lowest in vitro shut-off temperature, namely the cpts-248 (38 degree C) and cpts-530 (39 degree C) mutants, were the most restricted of the nine cp-**RSV** mutant progeny tested for efficiency of replication in Balb/c mice. In seronegative chimpanzees, the cpts-248 mutant replicated fourfold less efficiently in the nasopharynx and caused significantly less rhinorrhoea than its cp-**RSV** parent. The cpts-248 mutant virus, like its cp-**RSV** parent, was 1000-fold restricted in replication in the trachea compared with wild-type **RSV** . Previously, another candidate **RSV** live attenuated vaccine strain, a mutant designated ts-1, exhibited some instability of its ts phenotype following replication in susceptible humans or chimpanzees. Hence, we sought cp-**RSV** ts progeny that exhibited a greater degree of stability of the ts phenotype than the prototype ts-1 mutant. The cpts-248 and cpts-530 progeny viruses exhibited a greater degree of stability of the ts phenotype in nude mice than the ts-1 virus, and in chimpanzees, the former mutant also exhibited a greater stability of its ts phenotype than ts-1. The cpts-248 mutant was immunogenic and induced a high level of resistance in chimpanzees to subsequent challenge with wild-type **RSV** . The cpts-248 mutant therefore exhibits a set of properties that make it a promising vaccine candidate. These desirable properties of cpts-248 suggest that the mutant should be tested in humans for its suitability in immunoprophylaxis.

1994

36/3,AB/19 (Item 18 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

09230715 BIOSIS NO.: 199497239085
An update on approaches to the development of respiratory syncytial virus **(RSV) and parainfluenza virus type 3 (PIV3) vaccines.**
AUTHOR: **Murphy Brian R** (a); Hall Susan L; Kulkarni Arun B; Crowe James E Jr; Collins Peter L; Connors Mark; Karron Ruth A; Chanock Robert M
AUTHOR ADDRESS: (a)Lab. Infect. Dis., Natl. Inst. Allergy Infect. Dis., Natl. Inst. Health, Bethesda, MD**USA
JOURNAL: Virus Research 32 (1):p13-36 1994
ISSN: 0168-1702
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **RSV** and PIV3 are responsible for about 30% of severe viral respiratory tract disease leading to hospitalization of infants and children. For this reason, there is a need to develop vaccines effective against these viruses. Since these viruses cause severe disease in early infancy, vaccines must be effective in the presence of maternal antibody. Currently, several strategies for immunization against these viruses are being explored including peptide vaccines, subunit vaccines, vectored vaccines (e.g., vaccinia-**RSV** or adenovirus-**RSV** recombinants), and live attenuated virus vaccines. The current status of these approaches is reviewed. In addition, the immunologic basis for the disease potentiation seen in vaccinees immunized with formalin-inactivated **RSV** during subsequent **RSV** infection is reviewed. The efficacy of immunization in the presence of maternal antibody is discussed. Much progress for a **RSV** and PIV3 vaccine has been made and successful immunization against each of these pathogens should be achieved within this decade.

1994

36/3,AB/21 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09081403 BIOSIS NO.: 199497089773
A comparison in chimpanzees of the immunogenicity and efficacy of live attenuated respiratory syncytial virus **(RSV) temperature-sensitive mutant vaccines and vaccinia virus recombinants that express the surface glycoproteins of** RSV.
AUTHOR: Crowe James E Jr(a); Collins Peter L; London William T; Chanock Robert M; **Murphy Brian R**
AUTHOR ADDRESS: (a)Respiratory Viruses Section, Lab. Infectious Disease, Natl. Inst. Allergy Infectious Diseases, N**USA
JOURNAL: Vaccine 11 (14):p1395-1404 1993
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **Respiratory syncytial virus** (**RSV**) is the most common cause of viral bronchiolitis and pneumonia in children. The present study compares the level of attenuation, genetic stability and efficacy of three conditional-lethal temperature-sensitive (ts) mutants of the **RSV** A2 wild-type virus, designated ts-1, ts-1-NG1, and ts-4, in seronegative chimpanzees and also compares their efficacy with that of vaccinia virus recombinants that express the surface glycoproteins of **RSV** . Each of the

ts mutants was highly attenuated in the lower respiratory tract, but still retained the capacity to induce significant rhinorrhoea. Each of the three ts mutants underwent partial reversion to a non-ts (ts+) phenotype during replication in a minority of the chimpanzees. The ts+ virus present in the upper respiratory tract of the chimpanzees did not spread to the lower respiratory tract and represented only a minority fraction of the virus present in the nasopharyngeal swab specimens. The ts mutants were highly immunogenic and provided resistance that effectively restricted **RSV** replication following virus challenge. In contrast, the vaccinia-**RSV** recombinants were less immunogenic. They protected the lungs of two of four chimpanzees challenged with **RSV** , but failed to protect the upper respiratory tract. The chimpanzee can serve as a model for the rapid evaluation of further attenuated live **RSV** vaccines.

1993

36/3,AB/33 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08298594 BIOSIS NO.: 000043053592
SERIOUS RESPIRATORY TRACT DISEASE CAUSED BY RESPIRATORY SYNCYTIAL VIRUS **PROSPECTS FOR IMPROVED THERAPY AND EFFECTIVE IMMUNIZATION**
AUTHOR: CHANOCK R M; PARROTT R H; CONNORS M; COLLINS P L; **MURPHY B R**
AUTHOR ADDRESS: BUILD. 7, ROOM 100, 9000 ROCKVILLE PIKE, BETHESDA, MD. 20892.
JOURNAL: PEDIATRICS 90 (1 PART 2). 1992. 137-143. 1992
FULL JOURNAL NAME: Pediatrics
CODEN: PEDIA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1992

36/3,AB/94 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0190747 DBA Accession No.: 96-01518
Production of infectious human respiratory- syncytial virus **from cloned cDNA confirms an essential role for the transcription elongation factor from the 5' proximal open reading frame- of the M2 mRNA in gene expression and provides a capability for vaccine development; vector development for respiratory tract gene therapy**
AUTHOR: Collins P L; Hill M G; Camargo E; Grosfeld H; Chanock R M; **Murphy B R**
CORPORATE AFFILIATE: Nat.Inst.Allergy+Infec.Dis.Bethesda
CORPORATE SOURCE: Laboratory of Infectious Diseases, 7 Center Drive, MSC 0720, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892-0720, USA.
JOURNAL: Proc.Natl.Acad.Sci.U.S.A. (92, 25, 11563-67) 1995
ISSN: 0027-8424 CODEN: PNASA6
LANGUAGE: English
ABSTRACT: Infectious human **respiratory -syncytial virus** (**RSV**) was produced by the intracellular coexpression of 5 plasmid-borne cDNAs. One cDNA encoded a complete positive-sense version of the **RSV** genome, and each of the other 4 encoded major nucleocapsid N protein, nucleocapsid P phosphoprotein, major polymerase L protein or the protein from a 5' proximal open reading frame of M2 mRNA. A HEp-2

monolayer cell culture was infected with recombinant MVA vaccinia virus (1 focus-forming unit/cell) expressing phage T7 RNA-polymerase and transfected with antigenome N and P plasmids and L and M2 plasmids using LipofectACE. On day 3, clarified medium supernatants were passaged onto fresh HEp-2 cells and overlaid with methylcellulose (for subsequent antibody staining) or agarose (for plaque isolation). **RSV** may be used in vaccine and vector development for respiratory tract gene therapy. (21 ref)

36/3,AB/97 (Item 3 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00334272
ATTENUATED RESPIRATORY SYNCYTIAL VIRUS **VACCINE COMPOSITIONS**
COMPOSITIONS DE VACCINS A BASE DE VIRUS RESPIRATOIRE SYNCYTIAL ATTENUE
Patent Applicant/Assignee:
AMERICAN HOME PRODUCTS CORPORATION
THE UNITED STATES OF AMERICA as represented by THE DEPARTMENT OF HEALTH
Inventor(s):
MURPHY Brian Robert
CHANOCK Robert Merritt
CROWE James Earl Jr
CONNORS Mark
HSU Kuo-Hom Lee
DAVIS Alan Robert
LUBECK Michael David
SELLING Bernard Hugh
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English Abstract
The present invention provides vaccine compositions of attenuated **respiratory syncytial virus** (**RSV**). More particularly, the attenuated virus may be a derivative of **RSV** which has been incompletely attenuated by cold-passage or introduction of mutations which produce virus having a temperature sensitive (t s) or cold adapted (c a) phenotype. The invention also provides methods for stimulating the immune system of an individual to induce protection against **respiratory syncytial virus** by administration of attenuated **RSV** . The invention also provides pure cultures of attenuated RS virus, wherein the virus has been more completely attenuated by the further derivatization of previously identified incompletely attenuated t s or c p mutants

Japanese Abstract
L'invention concerne des compositions de vaccins a base de virus respiratoire syncytial (VRS) attenue. Ce virus attenue peut plus precisement etre un derive de VRS incompletement attenue par passage au froid ou par introduction de mutations donnant des virus dotes d'un phenotype sensible a la temperature (s t) ou adapte au froid (a f). L'invention concerne aussi des procedes visant a stimuler le systeme immunitaire d'un individu pour induire une protection contre le virus respiratoire syncytial par l'administration de VRS attenues. L'invention

concerne enfin des cultures pures de VRS attenues ou le virus a ete plus completement attenue par derivation ulterieure de mutants s t ou a f incompletement attenues comme indique precedemment.

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